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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,682	06/03/2005	Jacques F. Banchereau	BHCS:1028	8543

34725 7590 08/24/2010
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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
08/24/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,682	BANCHEREAU ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks filed 5/24/10 are acknowledged.

2. Claims 44-50 are under examination.

3. The amended Title has been entered and the objection to it has been withdrawn.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 44-50 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As set forth previously, the claims are vague and indefinite in the recitation of "TNFα". Regarding "TNFα", the specification defines TNFα as, "any TNF or TNF-like protein which functions as an activator in the methods of this invention". By this definition it is unclear then if Applicant is attempting to define other cytokines such as IL-4 as TNFα, given that IL-4 has the same effect on monocytes in the claimed method. Accordingly, the metes and bounds of the claims cannot be determined.

Applicant's arguments, filed 5/24/10, have been fully considered but are not found persuasive. Applicant argues a willingness to amend the claims.

Upon the submission of amendments to the claims the rejection will be reconsidered.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 44-50 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

A set forth previously, There is insufficient written description to show that Applicant was in possession of the tumor necrosis factor alpha (TNFα) of the claims.

At page 17 the specification defines TNFα as, "any TNF or TNF-like protein which functions as an activator in the methods of this invention". A review of the specification shows that even the TNFα employed in the Examples, e.g., page 21, is undefined as to its particular source, i.e., species or whether or not it is actually TNFα or a TNF-like protein. Clearly then no species of the thousands of TNFα's are actually described. No common TNFα structure is defined and neither is a common function. While it could be assumed that the common function might be the ability to induce the differentiation of monocytes into dendritic cells (DCs), the specification merely discloses that TNFα's, "function as an activator in the methods of this invention". Regarding the "TNF-like proteins" of the claimed method, none are defined nor disclosed. Clearly, neither specific structure and function, nor an adequate number of representative species of TNFα, are disclosed in the instant specification. One of skill in the art would therefore conclude that the specification fails to adequately describe TNFα. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

Applicant's arguments, filed 5/24/10, have been fully considered but are not found persuasive. Applicant argues a willingness to amend the claims.

Upon the submission of amendments to the claims the rejection will be reconsidered.

8. Claims 44-50 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth previously, The instant claims encompass a method for generating DCs from monocytes employing GM-CSF and TNFα. This method has been tried in the prior art and did not result in mature DCs. See Pickl et al. (1996) wherein the authors compared the resulting products of monocytes matured in GM-CSF and IL-4 to the products of monocytes matured in GM-CSF and TNFα. As stated in the Abstract, "Only GM-CSF plus IL-4 cultured cells [monocytes] were found to be potent stimulators in allogeneic and autologous MLR…", i.e., only the GM-CSF plus IL-4 cultured cells were mature DCs. At page 3853 and Figure 5 the reference further teaches that the GM-CSF and TNFα cultured monocytes appeared to be proliferating, which would not be a characteristic of mature DCs. Figure 9 shows that GM-CSF and TNFα cultured monocytes were only minimally better stimulators of

primary T cell responses than were freshly isolated monocytes. It appears then that culture of monocytes in GM-CSF and TNFα results in only partially differentiated DCs and not the mature DCs of the claims.

Applicant's arguments, filed 5/24/10, have been fully considered but are not found persuasive. Applicant argues a that Pickl et al. teach a failure of GM-CSF/TNFα-matured monocytes to activate T cells in an allogeneic MLR whereas the instant invention comprises the production of mature DCs from monocytes employing GM-CSF/TNFα in an antigen-specific context.

It is well-established that activation of T cells in an MLR context is much easier to perform than the activation of T cells in an antigen-specific context. To put it differently, if the GM-CSF/TNFα-matured monocytes of the reference failed to activate T cells in an allogeneic MLR it is highly unlikely that they would be capable of activating T cells in an antigen-specific context.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10. Claims 44-46 stand rejected under 35 U.S.C. 102(e) as being clearly anticipated by U.S. Patent No. 6,479,286.

As set forth previously, The '286 patent teaches a method of producing antigen loaded mature DCs comprising the step of maturing monocytes in GM-CSF and TNFα (see particularly Claim 3). Note that the monocytes can be transfected with a gene encoding an antigen of interest thus, producing "the presence of a pre-processed antigenic material" (see particularly column 15).

Applicant's arguments, filed 5/24/10, have been fully considered but are not found persuasive. Applicant argues that Claim 3 of the reference fails to teach the combination of GM-CSF and TNFα.

Claim 1 of the reference recites incubating monocytes in GM-CSF. Claim 3 recites, "further comprising incubating the dendritic cells with TNFα". Thus, the claim recites incubating the monocytes, as they mature into fully mature DCs, in GM-CSF and TNFα.

Applicant argues that the instant claims do not include the limitation that the cells are transduced to express antigen.

As set forth in the rejection, the monocytes can be transfected with a gene encoding an antigen of interest, thus, meeting the limitations of the claims that the cells are matured in the, "presence of an antigenic material".

11. Claims 44-47, 49, and 50 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Romani et al. (1994).

As set forth previously, Romani et al. teaches a method of producing antigen loaded mature DCs comprising the step of maturing cord blood mononuclear cells in GM-CSF and TNFα (see particularly page 85). Note that as the DCs matured they would have inherently loaded themselves with antigen. As cord blood comprises T cells as well as monocytes Claim 49 is included in the rejection. As any cell culture would inherently include some cell fractions and dying cell bodies Claim 50 is included in the rejection. As the cell culture medium comprised heat treated FCS, which inherently comprises some antigenic material, (see particularly page 84) Claim 47 is included in the rejection.

Applicant's arguments, filed 5/24/10, have been fully considered but are not found persuasive. Applicant argues that Romani teaches that TNFα was not essential and that the cells were not exposed to antigen.

Applicant is reminded that the rejection is under 35 U.S.C. 102(b) thus, arguments such as the reference teaches that TNFα was not essential and that the reference teaches away from the claimed method are irrelevant. At page 84, column 1 (and in other cites) the reference teaches that cord blood incubation was performed in GM-CSF and TNFα. Further, absent incubation in buffer alone, the maturing cells would inherently be incubated with antigenic material if only from dying cell fractions. It

is well-established that the maturing DCs would pick up, and become “loaded with”, any antigenic material in which they came in contact. Note that this concept must be the basis for the limitations of instant Claims 46 and 50. Regarding the “immune response” of Applicant’s argument, the instant claims recite no "immune response" limitation, thus, Applicant's argument is irrelevant.

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on (571) 272-0841.

15. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

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